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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/738,444	12/15/2000	William E. Jack	NEB-180	9633

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EXAMINER
LU, FRANK WEI MIN

ART UNIT	PAPER NUMBER
1655	5

DATE MAILED: 12/19/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/738,444	JACK ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *6-13 and 19-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 14-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/15/2000 (orginal)* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Location of Application

1. The Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1655.

Election/Restriction

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-5 and 14-18, drawn to a method for creating a target single-stranded region in double-stranded DNA (claims 1-5), classified in class 435, subclass 6; and a nucleic acid molecule (claims 14-16), a circular nucleic acid molecule (claim 17), and a DNA vector (claim 18), classified in class 536 , subclass 23.1.

II. Claims 6-11 and 13, drawn to a method of joining nucleic acid molecules (claims 6-11) and a method for producing a branched nucleic acid molecule (claim 13), classified in class 435, subclass 6.

III. Claim 12, drawn to a method for the purification of a specific DNA fragment , classified in class 435, subclass 6.

IV. Claim 19, drawn to a method for assembling a vector with multiple, interchangeable parts, classified in class 435, subclass 6.

V. Claims 20 and 21, drawn to a method for generating a DNA fragment with specific single-stranded termini, classified in class 435 , subclass 6.

3. The inventions are distinct, each from the other because of the following reasons:

Groups I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the method in Group I and Group II are different since they have different modes of operation, different functions, or different effects.

Groups I and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the method in Group I and Group III are different since they have different modes of operation, different functions, or different effects.

Groups I and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the method in Group I and Group IV are different since they have different modes of operation, different functions, or different effects.

Groups I and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the method in Group I and Group V are different since they have different modes of operation, different functions, or different effects.

Groups II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, these inventions are directed to different methods that have different modes of operation, different functions, or different effects.

Groups II and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, these inventions are directed to different methods that have different modes of operation, different functions, or different effects.

Groups II and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, these inventions are directed to different methods that have different modes of operation, different functions, or different effects.

Groups III and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, these inventions are directed to different methods that have different modes of operation, different functions, or different effects.

Groups III and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, these inventions are directed to different methods that have different modes of operation, different functions, or different effects.

Groups IV and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, these inventions are directed to different methods that have different modes of operation, different functions, or different effects.

Because these inventions are distinct for the reasons given above and the search required for Group II such as joining nucleic acid is not required for Group I, the search required for Group III such as purification is not required for Groups I , II, IV and V, the search required for Group IV such as a replication origin is not required for Groups I to III and V, the search required for Group V such as inserting a target DNA fragment between two sets of site-specific nicking sites is not required for Groups I to IV, restriction for examination purposes as indicated is proper.

During a telephone conversation with Mr. Gregory Williams (Reg. No. 30,901) on November 6, 2001 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-5 and 14-18. Affirmation of this election must be made by applicant in

replying to this Office action. Claims 6-13 and 19-21 have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Drawings

4. The drawings are objected to for reasons as stated on FORM PTO-948 (Rev. 8-98). Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect can be deferred until the application is allowed by the examiner.

Sequence Rules Compliance

5. The original filed sequencing listing has complied with Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Claim Objections

6. Claim 1 is objected to because of the following informality: "double-stranded DNA" should be "a double-stranded DNA".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-5 and 14-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Note that claims 2-5 and 14-18 are dependent on claim 1.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: creating a target single-stranded region in a double-stranded DNA.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1, 2, and 14-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Xu *et al.,* (US Patent No. 5,786,195, published on July 28, 1998).

Xu *et al.,* teach a method for cloning and producing the bssHII restriction endonuclease in *E. coli.*

Regarding claims 1 and 2, *B. stearothermophilus* H3 genomic DNA was digested with a restriction enzyme such as AciI or HinfI. Then the digested DNA samples (less than 10 kb) were self-ligated at a low DNA concentration (less than 2 microgram per ml). The ligated circular DNA was extracted and used as templates for inverse PCR reactions. PCR products were found in AciI or HinfI digested and self-ligated genomic DNA (for example, see column 9). Note that: (1) AciI or HinfI could be considered as a site-specific nicking endonuclease since DNA fragments produced by both restriction enzymes had 5' and 3' protruding, cohesive termini (a single-stranded region in a double-stranded DNA as recited in claim 1, for AciI and HinfI cut sites, see New England Biolabs 96/97 Catalog, pages 13 and 36); (2) *B. stearothermophilus* H3 genomic DNA had at least two sites of AciI or HinfI as recited in claim 2 since the fragments digested with AciI or HinfI were less than 10 kb (see above); and (3) the denaturation step in PCR could be considered as step (b) as recited in claims 1 and 2.

Regarding claims 14-18, DNA fragments produced by AciI or HinfI could be considered as a nucleic acid molecule as recited in claims 14-16 wherein each fragments have three double stranded subfragments (considered digested fragment as three parts) and two single-stranded termini (3' and 5' protruding, cohesive termini produced by AciI or HinfI) while the ligated circular DNA could be considered as a circular nucleic acid molecule as recited in claim 17

having at least two double stranded subfragments (considered the ligated circular DNA as two or more parts) and two single-stranded termini (3' and 5' protruding, cohesive termini produced by AciI or HinfI).

Regarding claim 18, although Xu *et al.,* did not directly show the double digestion of a pLG339 vector with Xba I and BamHI, in the absence of convincing evidence to the contrary, this limitation could be considered to be inherent to the reference taught by Xu *et al.,* since this vector was used to clone bssHIIR gene PCR amplified in the presence of a forward primer with a Xba I site and a reverse primer with a BamHI site (see column 10). The protruding, cohesive termini in the pLG339 vector produced by Xba I/BamHI digestion could be considered as two single stranded termini (for sites of Xba I and BamHI, see New England Biolabs 96/97 Catalog, pages 17 and 53).

Although the nucleic acid molecules recited in claims 14-18 were not produced by the method of claim 3, it was well established that even though product-by process claims were limited by and defined by the process, the determination of the patentability of the product was based on the product itself. The patentability of a product did not depend on its method of production. If the product in the product-by-process claim was the same as or obvious from a product of the prior art, the claim would be unpatentable even though the prior product was made by a different process."*In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

Therefore, Xu *et al.,* teach all limitations recited in claims 1, 2, and 14-18.

11. Claims 1-5 and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Alland *et al.,* (Proc. Natl. Acad, Sci. USA, 95, 13227-13232, October 1998).

Alland *et al.,* teach identification of differentially expressed mRNA in prokaryotic organisms by customized amplification libraries (DECAL).

Regarding claims 1-5, purified cosmid DNA digested with PacI was further digested with AluI. Then the section corresponding to 400-1,500 bp of the AluI digest was collected and was ligated with XhoI adapters. Finally the ligated product was used for PCR (see left column in page 13228 and Figure 1 in page 13229). Note that: (1) PacI and Alu I could be considered as site-specific nicking endonucleases; (2) purified cosmid DNA digested with PacI could be considered as a double stranded DNA having two breaks located on the border of target region of its second strand as recited in claims 3-5 since DNA fragments produced by PacI digestion had 5' and 3' protruding, cohesive termini (a single-stranded region in a double-stranded DNA as a break of a double stranded DNA, for Pac cut site, see New England Biolabs 96/97 Catalog, page 43); (3) purified cosmid DNA digested with PacI could be considered to have three or more Alu sites (three or more Alu subfragments) as recited in claims 1, 2, and 14-16 since 400-1,500 bp DNA fragments were generated after AluI digestion; (4) the ligated product had 5' and 3' protruding, cohesive termini (a single-stranded region in a double-stranded DNA, for Xho I site, see New England Biolabs 96/97 Catalog, page 54); and (5) the denaturation step in PCR could be considered as step (b) as recited in claims 1-3.

Although the nucleic acid molecules recited in claims 14-16 were not produced by the method of claim 3, it was well established that even though product-by process claims were

limited by and defined by the process, the determination of the patentability of the product was based on the product itself. The patentability of a product did not depend on its method of production. If the product in the product-by-process claim was the same as or obvious from a product of the prior art, the claim would be unpatentable even though the prior product was made by a different process."*In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

Therefore, Alland *et al.,* teach all limitations recited in claims 1-5 and 14-16.

12. Claims 1, 17, and 18 are rejected under 35 U.S.C. 102(a) as being anticipated by Wang *et al.,* (Molecular Biotechnology, 15, 97-104, June, 2000).

Wang *et al.,* teach the preparation of DNA substrates for in Vitro mismatch repair. As shown in Figure 1, a vector pUC19XE was nicked with N.Bst NBI and then denatured and reannealed with a denatured pUC18HE (see page 100). Note that: (1) the denaturation step could be considered as step (b) as recited in claim 1; and (2) the nicked vector pUC19XE could be considered to have three or more subfragments with 3' and 5' termini since this vector could be divided into three or more parts.

Although the nucleic acid molecules recited in claims 17 and 18 were not produced by the method of claim 3, it was well established that even though product-by process claims were limited by and defined by the process, the determination of the patentability of the product was based on the product itself. The patentability of a product did not depend on its method of production. If the product in the product-by-process claim was the same as or obvious from a

product of the prior art, the claim would be unpatentable even though the prior product was made by a different process."*In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

Therefore, Wang *et al.,* teach all limitations recited in claims 1, 17, and 18.

Conclusion

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Higashitani *et al.,* J. Mol. Biol., 237, 388-400, 1994 (at least read claims 1 and 2).

14. No Claim is allowed.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
December 13, 2001

ETHAN C. WHISENANT
PRIMARY EXAMINER